ABSTRACT

A novel gene defining a novel human UDP-GlcNAc: Galβ1-3GalNAcα β1,6GlcNAc-transferase, termed C2GnT3, with unique enzymatic properties is disclosed. The enzymatic activity of C2GnT3 is shown to be distinct from that of previously identified enzymes of this gene family. The invention discloses isolated DNA molecules and DNA constructs encoding C2GnT3 and derivatives thereof by way of amino acid deletion, substitution or insertion exhibiting C2GnT3 activity, as well as cloning and expression vectors including such DNA, cells transfected with the vectors, and recombinant methods for providing C2GnT3. The enzyme C2GnT3 and C2GnT3 -active derivatives thereof are disclosed, in particular soluble derivatives comprising the catalytically active domain of C2GnT3. Further, the invention discloses methods of obtaining 1,6-N-acetylglucosaminyl glycosylated saccharides, glycopeptides or glycoproteins by use of an enzymically active C2GnT3 protein or fusion protein thereof or by using cells stably transfected with a vector including DNA encoding an enzymatically active C2GnT3 protein as an expression system for recombinant production of such glycopeptides or glycoproteins. Methods are disclosed for the identification of agents with the ability to inhibit or stimulate the biological activity of C2GnT3. Furthermore, methods of using C2GnT3 in the structure-based design of inhibitors or stimulators thereof are also disclosed in the invention. Also a method for the identification of DNA sequence variations in the C2GnT3 gene by isolating DNA from a patient, amplifying C2GnT3-coding exons by PCR, and detecting the presence of DNA sequence variation, are disclosed.